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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/091,360	03/04/2002	Petros Tsipouras	IK-110.3(C)	1541
47670 7590 02/10/2006 KELLEY DRYE & WARREN LLP TWO STAMFORD PLAZA 281 TRESSER BOULEVARD STAMFORD, CT 06901			EXAMINER CLOW, LORI A	
			ART UNIT	PAPER NUMBER
			1631	

DATE MAILED: 02/10/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 10/091,360	Applicant(s) TSIPOURAS ET AL.	
	Examiner Lori A. Clow, Ph.D.	Art Unit 1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 09 November 2005.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 13-18,31-34 and 36-43 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 13-18,31-34 and 36-43 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Applicants' arguments, filed 11 November 2005, have been fully considered. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

Claims 13-18, 31-34, and 36-43 are currently pending in the application.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 13-18, 31-34, and 36-43 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 38 recites "forming the rare cell image color signal" at step (iii). There is insufficient antecedent basis in the claim for "the rare cell image". Perhaps Applicant intends the claim to read "forming a rare cell image". Clarification is requested.

Claims 38 and 39, step (iii), are indefinite. The amended claims now reads "wherein rare cell image color signal characteristic values which may serve as predetermined rare cell image selection criteria appear more prominently in one or more coordinate signal thereof". It is unclear what is intended by this step. First, there is insufficient antecedent basis for "color signal characteristic". No characteristic has been previously identified. Secondly, what is a predetermined rare cell image selection criteria? This is not defined. What does it appear more

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prominently than? Thirdly, the “characteristic *may* serve as predetermined rare cell image selection criteria”. This is unclear. Is this a positive method step? Clarification is requested.

Claims 38 and 39 recite “and identify the rare cell image”. What identifies the rare cell image? Is it the mask that is the rare cell image or is it the “blob” without portions thereof”. This is not clear. What parameters, taken from the listed steps, actually identify a rare cell image? Clarification is requested.

Claim 39, step (iii), reads “wherein rare cell image color signal characteristic values which may serve as predetermined rare cell image selection criteria appear more prominently in one or more coordinate signal thereof”. It is unclear what is intended by this step. What is a predetermined rare cell image selection criteria? This is not defined. Second, the “characteristic *may* serve as predetermined rare cell image selection criteria”. This is unclear. Is this a positive method step? Clarification is requested.

Claim 14 recites “the method of claim 13, wherein the step of creating a selected rare cell signal further comprises”. There is no step, in the parent claim, of “creating a selected rare cell signal”. There is a step of selecting, for processing, rare cell signal points. There is also step (iv) which produces a “rare cell image mask signal”. Clarification is requested.

Claim 14 recites “applying to the selected signal points a closing filter, applying a hole filling function, and excluding areas including a border of the image, an erosion filter is applied, and a thick filter is applied, producing the selected rare cell signal”. First, this is grammatically incorrect. It is unclear, from the manner in which this is written, where the erosion filter is applied. Is it applied after the hole filling function or to the hole filling function? Clarification is requested.

Claim 17 recites “with a rare cell area from the rare cell data set”. There is insufficient antecedent basis in the claim for “rare cell data set”. There is no rare cell data set mentioned in a previous claim. Clarification is requested.

Claim 31 recites “the step of producing creating a rare cell color image”. This is confusing, as there is only a step of producing an image mask in claim 39. It is unclear what Applicant intends. There is no step of producing or creating a rare cell color image. The claim is drawn to a computer software product comprising a computer-readable storage medium containing a sequence of computer directed steps to selectively **identify** a rare cell image. Clarification is requested.

Claim 32 recites “the step of creating a selected a rare cell image signal”. There is no step of creating a selected rare cell image. Rather, the step is one of producing a rare cell image **mask**. This is indefinite, as it is unclear what Applicant intends by this step. Clarification is requested.

Claim 33 recites “the step of producing a selected a rare cell image signal”. There is no step of producing a selected rare cell image. Rather, the step is one of producing a rare cell image **mask**. This is indefinite, as it is unclear what Applicant intends by this step. Clarification is requested.

Claims 31-33 recite “the product of claim 39, wherein the step of”. This is unclear, as the product is a physical thing. Does Applicant intend that the product contain instructions which comprise steps? Clarification is requested.

Claim 36 recites “the rare cell data set”. There is insufficient antecedent basis in the claim for the “data set”. Clarification is requested.

Claim 37 recites “the method of claim 39”. This is unclear, as claim 39 is directed to a product. Clarification is requested.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claims 38, 39, and 40-43 are rejected under 35 U.S.C. 102(a) as being anticipated by WO 97/20198 (Douglass et al.).

Independent claims 38 and 39 are drawn to a computer-controlled method and a computer software product with instructions for rare cell image identification comprising receiving a color image signal of an unenriched body fluid or tissue sample, transforming the color image signal from RGB to HLS magnitude, wherein a candidate blob may be identified, forming the rare cell image color signal, and producing a mask, which eliminates portions not defining the rare cell.

In regard to claims 38 and 39, Douglass et al. teach a method and apparatus for automated cell analysis of biological specimens to acquire images of candidate objects of interest (abstract). Douglass teaches that the method may be used for rare cell identification, such as fetal cells in maternal blood (page 3, line 4). The processing begins via transformation of the image to a different color space (page 3, lines 7-8). This entails receiving images through a microscope subsystem, linked to a camera, in which the image comprises pixels which comprise

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red, green and blue (RGB) signal values. It is desirable to transform the RGB values to a different color space. This can include the transformation to hue, saturation, and intensity (HIS). (Intensity and luminescence are equivalent) (page 16, lines 4, 30-34; page 18, lines 6-13). An image mask is applied to the signal using a low pass filter to obtain only the object of interest and nothing else (page 19, lines 17-26).

In regard to claims 40 and 42, Douglass teaches computer aligned microscope image acquisition (page 5, lines 24-32).

In regard to claims 41 and 43, Douglass teaches that method and apparatus may be used for rare event detection in which the object of interest may only be present at a ratio of one to several hundred thousand normal cells (page 6, lines 13-15).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 13-18, 31-34, and 36-39 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 97/20198 (Douglass et al.), in view of Glasbey et al. (Image Analysis for the Biological Sciences (1995) John Wiley and Sons, Chichester, England, pages 31-33).

Independent claims 38 and 39 are drawn to a computer-controlled method and a computer software product with instructions for rare cell image identification comprising receiving a color image signal of an unenriched body fluid or tissue sample, transforming the color image signal from RGB to HLS magnitude, wherein a candidate blob may be identified, forming the rare cell image color signal, and producing a mask, which eliminates portions not defining the rare cell.

In regard to claims 38 and 39, Douglass et al. teach a method and apparatus for automated cell analysis of biological specimens to acquire images of candidate objects of interest (abstract). Douglass teaches that the method may be used for rare cell identification (claims 16-18, 34, 36, and 37), such as fetal cells in maternal blood (page 3, line 4). The processing begins via transformation of the image to a different color space (page 3, lines 7-8). This entails receiving images through a microscope subsystem, linked to a camera, in which the image

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comprises pixels which comprise red, green and blue (RGB) signal values. It is desirable to transform the RGB values to a different color space. This can include the transformation to hue, saturation, and intensity (HIS). (Intensity and luminescence are equivalent) (page 16, lines 4, 30-34; page 18, lines 6-13). An image mask is applied to the signal using a low pass filter to obtain only the object of interest and nothing else (page 19, lines 17-26).

Douglass teaches that image processing includes color space conversion, low pass filtering, background suppression, artifact suppression, morphological processing, and blob analysis. One or more of these steps can be performed, as the operator sees fit. Douglass does not specifically teach the rare cell image mask filtering by histogram analysis, as presented in claims 13-15 and 31-33, however, Glasbey teaches the basic principals of image analysis, including histogram filtering. Glasbey describes application of a histogram equalization for image transformation such that all display intensities are equally represented (page 31). The intention is that the ranges of pixel values are allocated portions of the display intensity ranges according the frequency with which they occur in the image (see Figures 2.7 (a) and (b)). The calculation is based upon the minimum and maximum values represented as a histogram (peaks and valleys) (see algorithm on page 32).

It would have been prima facie obvious to one of ordinary skill in the art at the time of the invention to have used the histogram technique of filtering, as taught by Glasbey, in the methods and apparatus of Douglass. One would have been motivated to do so because Douglass states that the image processing steps of low pass filtering, thresholding, etc. are generally known image processing building blocks (page 15, lines 30-34).

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Conclusion

No claims are allowed.

The outstanding rejections under 35 USC 112, 2nd paragraph have been withdrawn in view of Applicants arguments.

Prior Art Made of Record

The following prior art made of record and not relied upon is considered pertinent to applicant's disclosure: US 5,764,792 (Keannealy). Keannealy teaches the detection of rare cells from a biological sample, such as fetal cells in maternal blood samples (abstract). Keannealy does not teach the transformation of the color image signal from RGB to HLS or the rare cell image selection criteria.

Inquiries

Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the PTO Fax Center. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993) (See 37 CFR § 1.6(d)). The Central Fax Center Number is (571) 273-8300.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lori A. Clow, Ph.D., whose telephone number is (571) 272-0715. The examiner can normally be reached on Monday-Friday from 10 am to 6:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel, Ph.D., can be reached on (571) 272-0718.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the

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February 1, 2006

Lori A. Clow, Ph.D.

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Lori A. Clow

MARJORIE A. MORAN
PRIMARY EXAMINER

Marjorie A. Moran
2/2/06